REMARKS

Preliminary Remarks

Claims 107-111 and 117-132 are currently pending and are under examination. Claims 1-88, 89, and 102-106 were previously canceled. Applicants respectfully request entry of the remarks made herein into the file history of the present application.

Patentability Arguments

A. The Rejections of Claims 107-111 and 117-132 Under 35 U.S.C. §§ 103(a) Should Be Withdrawn

Claims 107-111 and 117-132 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Bram *et al.* (WO 98/39361) (hereinafter "Bram") in view of Presta et al. (U.S. Patent No. 5,739,277) (hereinafter "Presta") for "reasons set forth in the previous Office action in the rejection of claims 89 and 102-6 and 108-111." Applicants respectfully traverse these rejections in view of the following arguments.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, the Examiner must provide a clear articulation of the reasons why the claimed invention would have been obvious, i.e., the Examiner must provide a reason one of ordinary skill in the art would have combined the cited references to arrive at the claimed invention. Second, there must be a reasonable expectation of success. That is, the hypothetical person of ordinary skill in the art, at the time the invention was made, must have had a reasonable expectation that the proposed modification or combination would work to produce beneficial results. Finally, the references when combined must teach or suggest all the claim limitations. *See* MPEP § 2143. The burden of establishing a *prima facie* case of obviousness lies with the Examiner, and the expectation of success must be found in the prior art, not the applicant's disclosure." *In re Dow Chemical*, 5 USPQ 2d 1531 (Fed. Cir. 1988).

Applicants respectfully submit that the cited references, alone or in combination, fail to teach or suggest all the claim limitations. Moreover, Applicants respectfully submit that the Examiner applied an improper standard in finding the pending claims obvious. For at least these reasons, the Examiner has failed to establish a *prima facie* case of obviousness.

The specifically claimed fusion proteins comprising a first portion consisting of the claimed TACI fragments are simply not disclosed by Bram nor is any guidance provided therein

through which one of ordinary skill in the art might obtain such specific fusion proteins. The disclosure of Presta does nothing to rectify the failure of Bram to disclose the specifically claimed fragments. Because the specific, structurally defined TACI fragments are not disclosed in either Bram or Presta or any combination thereof, and because the allegedly obvious process for obtaining such fragments fails to fill the gap regarding the particular subject matter of the pending claims, the Examiner has failed to establish a *prima facie* case of obviousness.

The Examiner avers that "given that there (sic) Bram discloses the use of full length TACI extracellular domain (SEQ ID NO:6) and that there are a finite number of fragments of said extracellular domain and it would have been obvious to the skilled artisan to produce said fragments in order to identify the specific binding domain (fragment) of the TACI extracellular domain responsible for the observed biological activity." The Examiner's comments amount to an "obvious to try" standard, which is not the proper standard where, as here, the results are not predictable or identified. According to the U.S. Supreme Court in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007), "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of **identified, predictable solutions**, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." (emphasis added). Biological and chemical processes are unpredictable; as discussed below, the instant invention derives from an unpredictable result and therefore is not obvious.[1] This unpredictability has been explicitly acknowledged by the Examiner in prior Office communications. *See, e.g.*, Office communication mailed May 23, 2005 at page 22 (stating that "the art is unpredictable").

At the time of the instant invention it was not predictable that the specifically claimed TACI fragments would bind BLyS removed from the context of the full-length polypeptide. For example, the transmembrane domain of a variety of cell receptor proteins has been demonstrated to contribute to ligand binding.[2] Moreover, amino acids immediately adjacent to the

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[1] *See also Ortho-McNeil Pharmaceutical v. Mylan Labs*, 520 F.3d 1358 (Fed. Cir. 2008) (holding that the cited passage of *KSR* is applicable only in the case of an "easily traversed, small and finite number of alternatives" and is not properly applied if the alternatives are "unpredictable") (emphasis added).

[2] Mol. Cell. Biol. 24(5):2041-2051 (submitted herewith as Exhibit A) (2004) ("residues at the extracellular ends of transmembrane domains of G protein-coupled receptors have been found to contribute to ligand binding"); J. Biol.

transmembrane domain have been shown to play a crucial role in the proper folding of the extracellular domains of, and the ligand binding capacity of, several signal transducing proteins.[3] Thus, one of ordinary skill in the art would comprehend the inherent unpredictability with regard to the ability of the specifically disclosed and claimed fusion proteins to retain ligand binding capability as required by the instantly pending claims.

Moreover, while there may exist a finite number of fragments of the extracellular domain, the Examiner fails to appreciate the scope of possible fragments which extends at least into the thousands, precluding contemplation of or focus on the specifically claimed TACI fragments. Not a single such fragment is identified by Bram. In fact, Bram only makes a general statement that the ligand binding domain is located somewhere within the TACI extracellular domain. The reference does not disclose the currently claimed fragments, nor does Bram identify a TACI ligand which could be used to identify which, if any, of the thousands of extracellular fragments retain ligand binding capability. Thus, there is simply no way to predict from Bram that the currently claimed fragments would constitute ligand-binding fragments. The claimed fusion proteins cannot be obvious where the prior art does not lead the skilled artisan to the specifically claimed fragments especially given there is no ligand identified which could be used to identify such ligand binding fragments.

In summary, because Bram and Presta, individually or in combination, fail to teach or suggest the specifically claimed TACI fragments and because of the difficulty for one of ordinary skill in the art to identify the ligand binding property of such fragments without knowledge of the ligand's identity, the prior art cannot as a matter of law render the instant claims obvious and the rejection over Bram in view Presta under 35 U.S.C. § 103(a) should be withdrawn, and the withdrawal is respectfully requested

B. The Rejections for Obviousness-type Double Patenting

Chem. 271(34):20331-20339 (1996) (submitted herewith as Exhibit B) (describing a transmembrane region of somatostatin receptors 1 and 2 essential for ligand-binding)

[3] Diabetes 54 (Suppl. 2):S151-S158 (2005) (submitted herewith as Exhibit C) (G-to-T transversion at portion of extracellular domain immediately adjacent to transmembrane domain thought to affect nearby ligand binding domain of leptin receptor and reduce signaling through the receptor); Am. J. Respir. Cell. Mol. Biol. 32:498-503 (2005) (submitted herewith as Exhibit D) (intact Coxsackievirus B and Adenovirus Receptor extracellular domain required for efficient ligand binding and infection)(emphasis added); Infect. Immun. 64(12):5144-5150 (1996) (submitted herewith as Exhibit E) ("the region adjacent to the [guanylyl cyclase] transmembrane domain plays an important role in facilitating a favorable conformation...for heat stable enterotoxin binding.")

Claims 107-109, 117-119 and 122-123 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-4 of copending Application No. 11/748,978. Applicants wish to defer the response to these provisional rejections until the claims are otherwise allowable.

Conclusion

In view of the above remarks, applicants respectfully submit that the instant application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the (312) 595-1408. Should any additional fees be deemed necessary in connection with the filing of this document, the Commissioner is hereby authorized to deduct any such fees from Deposit Account No. 08-3038 referencing the above attorney docket number.

Respectfully submitted,

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